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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/611,748	06/30/2003	Narendra S. Yadav	CL1944USNA	4485

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EXAMINER	
MEHTA, ASHWIN D	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 09/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/611,748	YADAV, NARENDRA S.	
	Examiner	Art Unit	
	Ashwin Mehta	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *4,11,12,14-20 and 27-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5, 6, 8, 13, 21-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10152003 01022004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-3, 5-10, 13, and 21-26, species C (5' Intron-TS_{INV}-$P2_{INV}$) and species F (3' Intron-TS_{INV}-polyA) in the reply filed on July 31, 2006 is acknowledged. The traversal is on the ground(s) that the different structures identified in Groups I-III are variations upon a general methodology for conditionally regulating gene silencing with the use of site-specific recombination that result in the expression of dsRNA. Applicants therefore believe that the search for Group I will encompass the majority of the search for Groups II and III (response, pages 1-2). This is not found persuasive because the different structures give the methods of the different groups materially distinct designs. While each of the methods involves use of site-specific recombinase system, the modes of operation of the methods differ, because of the distinct designs. A search for structures used in the one of the methods will not produce structures used in the others. Note that claims 7, 9, and 10 do not read on the elected species, and are withdrawn for reading on a non-elected invention. Claims 1-3, 5, 6, 8, 13, and 21-26, species C (5' Intron-TS_{INV}-$P2_{INV}$) and species F (3' Intron-TS_{INV}-polyA) are examined in this Office action.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

2. Regarding the IDS filed October 15, 2003: the citation for EP 1115878 was lined through because a copy of the reference was not supplied. Regarding the IDS filed January 2, 2004: the

Odell et al. 1991 reference was lined through only because the same citation appears, and was initialed as considered, in the IDS filed October 15, 2003.

Claim Objections

3. Claims 5, 6, 13, and 21-26 are objected to for depending from non-elected claims.

4. Claim 23 is objected to because of the following informalities: the term "of" in "of thereof" in the last line should be deleted. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-3, 5, 6, 8, 13, and 21-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1 and 8: the recitation, "a second gene silencing-recombinase element" in line 6 renders the claims indefinite. The claims do not mention a first gene silencing-recombinase element.

Further in claims 1 and 8: there is insufficient antecedent basis for the recitation, "the target gene", recited in the last line.

In claim 13: the recitation, "germline" renders the claim indefinite. The specification on page 21, lines 15-20 states, "In the context of this invention, the germline goes through different

developmental stages starting, say, from fertilization through development of embryo, vegetative shoot apical meristem, floral shoot apical meristem, anther and pistil primordia, anther and pistil, micro- and macrospore mother cells, and macrospore (egg) and microspore (pollen)." The recitation, "say" is open language. While this statement provides examples of what is to be considered "germline" in the instant invention, it is unclear what other developmental stages are, and are not, considered "germline", making the metes and bounds of the claim unclear.

In claim 23: the recitation, "homologs [of] thereof" in the last line renders the claim indefinite. The specification indicates that many of the genes mentioned in parts a)-h) are homologs of each other (page 41, lines 15-17). It is then unclear exactly what genes are being referred to as homologs in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-3, 5, 6, 8, 13, 21, 22, and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (Nature, 2000, Vol. 407, pages 319-320) in combination with Odell et al. (WO 91/09957).

The claims are broadly drawn towards a gene silencing site-specific recombination system comprising a first recombinase element having the structure P1-R, wherein P1 is a first

promoter and R is a recombinase coding sequence and 3' region, and a gene silencing-recombinase element having the structure RS-X-RS*-Y, the elected species having the structure RS-5' Intron-TS_{INV}-$P2_{INV}$-RS*-3' Intron-TS_{INV}-polyA.

Smith et al. teach a method for silencing the expression of a specific target gene in a cell, comprising introduction of a construct that expresses a hairpin RNA comprising an intron. The arms of the hairpin comprise complementary nucleotide sequences, and are sense or antisense sequences that target the target gene. The arms of the hairpin are separated by an intron. The DNA sequences encoding the hairpin RNA are operably linked to the constitutive CaMV 35S promoter and the OCS terminator. Upon expression, pre-mRNA processing removes the intron, the sense and antisense nucleotide sequences form a dsRNA, and the target gene is silenced. The arm of the hairpin adjacent to the terminator encodes the antisense-oriented target sequence ("3'-5'"). One construct taught by Smith et al. target a viral gene, and confers immunity to the virus when expressed in plants. Another construct targets an endogenous delta12-desaturase gene, which catalyses the conversion of oleic acid to linoleic acid in seeds (page 320).

Smith et al. do not teach a site-specific recombination system.

Odell et al. teach the use of the Cre-lox site-specific recombination system to manipulate exogenous DNA once it is within a plant cell or plant, to control expression of the DNA. The exogenous DNA may encode a product that disrupts gene expression in plant cells, and are operably linked DNA segments that control expression, including promoters and polyadenylation sequences. The site-specific recombination event catalyzed by the Cre recombinase can cause the inversion of a DNA segment that comprises a promoter bound by lox sites in reverse orientation, such that the promoter goes form an inactive to an active orientation with respect to

the coding region to be transcribed (recombination sites). The DNA segments containing the Cre coding sequence operably linked to a promoter, and the DNA segments comprising the lox sites and DNA to be manipulated, can be in the same plasmid, and therefore "genetically linked" or in different plasmids and introduced into different plants (and therefore unlinked). Any type of promoters may be used with the system, including the constitutive CaMV 35S promoter, tissue-specific promoters, developmentally stage-specific promoters, promoters active during reproductive cell formation, safener-induced promoters (pages 3-5, 13-16, 18; claims). Given the indefiniteness of the term "germline" as used in the instant application (see the rejection above), the CaMV 35S promoter, as well as promoters active during reproductive cell formation, can be considered germline promoters.

It would have been obvious and within the scope of one of ordinary skill in the art at the time the invention was made to modify the hairpin RNA-encoding construct of Smith et al. to incorporate a site-specific recombination system, for example the Cre-lox system taught by Odell et al. It would have been obvious to place inversely oriented lox sites upstream of the promoter controlling expression of the hairpin and within the intron. These are DNA segments that control expression. Expression of the Cre recombinase would have led to the inversion of the promoter-5' intron segment, thereby allowing transcription of the hairpin RNA comprising a complete, spliceable intron. One of ordinary skill in the art would have been motivated to make such a modification, as it provides a way of controlling expression of exogenous DNA, as taught by Odell et al.

7. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (Nature, 2000, Vol. 407, pages 319-320) in combination with Odell et al. (WO 91/09957) as applied to claims 1-3, 5, 6, 8, 13, 21, 22, 24, 25, and 26 above, and further in view of Dalmay et al. (Cell, 2000, Vol. 101, pages 543-553).

Claim 23 limits the target gene to be a gene involved in gene silencing.

Smith et al. in combination with Odell et al. teach a vector system comprising a site-specific recombination system and expression of hairpin RNA to silence a target gene, as discussed above.

Smith et al. in combination with Odell et al. do not teach a gene involved in gene silencing.

Dalmay et al. teach isolation of the Arabidopsis SDE-1 gene, that it is required for transgene silencing but not virus-induced post-transcriptional gene silencing (pages 547-548).

It would have been obvious and within the scope of one of ordinary skill in the art at the time the invention was made to use the silencing system taught by Smith et al. in combination with Odell et al. as discussed above by targeting a gene involved in gene silencing in a host cell or plant, for example the SDE-1 gene, using sequences from the isolated gene taught by Dalmay et al. for the target sequences. One would have been motivated to target such a gene, to further study the gene silencing pathway of the host cell or organism.

Contact Information

Any inquiry concerning this or earlier communications from the Examiner should be directed to Ashwin Mehta, whose telephone number is 571-272-0803. The Examiner can normally be reached from 8:00 A.M to 5:30 P.M. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Anne Marie Grunberg, can be reached at 571-272-0975. The fax phone numbers for the organization where this application or proceeding is

assigned are 571-273-8300. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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August 28, 2006

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